Distinct profiles in frontotemporal dementia and frontal variant of Alzheimer disease.

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Background

Frontal variant of Alzheimer's disease (fvAD) represents a subgroup of AD with prominent behavioral abnormalities in the early stage of the disease, executive dysfunction and language impairment. fv-AD shares common clinical features with behavioral variant frontotemporal dementia (bvFTD), making differential diagnosis a major challenges.

Objective

Our purpose was to describe the distinguishing features between fvAD and bvFTD by comparing clinical, laboratory and instrumental data. We therefore collected clinical, neuropsychologic, brain magnetic resonance imaging (MRI), cerebrospinal fluid (CSF), and cerebral positron emission tomography (PET) findings in 3 fvAD and 3 bvFTD patients.

Materials and methods

We performed in each patient:

(a) a detailed clinical and neuropsychologic examination;

(b) CSF total tau (t-tau), phosphorylated tau (p-tau), beta-amyloid 42 (Aβ42) assessment;

(c) conventional brain MRI;

(d) (18)F-FDG cerebral PET on a high-resolution research tomograph;

(e) the subgroup of fvAD patients underwent (18)F-flumetamol amyloid-beta PET scans.

Results

All patients met the diagnostic criteria for possible bvFTD dementia, with prominent behavioural features present in all. Age at onset was quite homogeneous in both groups. In fv-AD patients neuropsycologic assessment showed greater memory and executive impairment and milder behavioral symptoms than in bvFTD patients. At onset, apathy was the most common behavioural feature in fvAD, while hyperorality and perseverative/compulsive behaviour was prevalent in bvFTD patients. Mini Mental State Examination (MMSE) score was higher in bvFTD respect to fv-AD. Conventional brain MRI showed a non specific pattern in all cases. CSF Aβ42 was significantly lower in fvAD compared to bvFTD, while CSF tau and p-tau were higher in fvAD. Notably, while CSF Aβ42/p-tau was normal in bvFTD, it was low in fvAD. (18)F-FDG cerebral PET showed in all cases a frontal-parieto-temporal hypometabolism, but with a different pattern in the two groups. Amyloid PET scans in the 3 fvAD confirmed the diagnostic suspicion showing marked amyloid deposition. These data are summarized in table 1.

Conclusion and discussion

Herein we reported the clinical, CSF, and imaging features of 6 patents with the two main frontal cortical dementias, and showed that bvFTD and fvAD present important differencies. The findings of this study highlight that detailed neuropsychological tests, CSF biomarkers, and functional neuroimaging will lead to greater accuracy in the diagnosis of these clinically overlapping syndromes and patient management.

Table 1: fv-AD *versus* bvFTD: a synopsis. **Legend:** *n.p.:* not performed; *WM*: white matter.

	fv-AD			bvFTD		
	Pt 1	**Pt 2**	**Pt 3**	**Pt 1**	**Pt 2**	**Pt 3**
Sex	F	M	F	M	M	F
Clinical onset (age)	59	58	68	68	60	59
MMSEc	10/30 (after 1 year of illness)	8/30 (after 6 years of illness)	18.7/30 (after 1 year of illness)	25.8 (after 3 years of illness)	19 (after 4 years of illness)	18 (after 3 years of illness)
CDR	2	2	1	0.5	2	2
Neuropsychological profile	Prevalent language deficit, dysesecutive	Amnesic multidomain	Amnesic multidomain	Dysesecutive	Multidomain	Dysesecutive
Symptom at onset	Behavioural (morbid jealousy)	Mood depression, apathy, memory impairment..	Memory impairment, spatial disorientation, apathy	Behavioural (change of character with episodes of aggression, apathy)	Behavioural, dysesecutive	Bahavioural (apathy, disinhibition, hyperphagia)
Clinical evolution	Rapid. Apraxia, aphasia.	Slow. Aggression, hyperphagia, pathological ideations.	Slow.	Slow. Attentional deficits, dysesecutive syndrome.	Slow.	Slow. Akathisia, incontinence, acholalia, no spontaneous speech.
MRI	Frontotemporal bilateral atrophy	Diffuse cortical atrophy	Frontoparietal bilateral atrophy	Anterior atrophy, WM lesions	Anterior atrophy, WM lesions	Frontotemporal atrophy.
FDG-PET	Aspecific	AD pattern	AD pattern	FTD pattern	FTD pattern	FTD pattern
Amyloid-PET	+++	++	+++	n.p.	n.p.	n.p.
CSF:						
Tau (n.v. <275 pg/ml)	1270	193	722	205	130	386
β-Amyloid (n.v. >600 pg/ml)	514	419	499	597	718	1117
pTau (n.v. <50 pg/ml)	178	39	113	30	27	47
βA/pTau	2.8	11	4.1	19	26.5	23.8
Tau/βA	2.47	0.46	1.54	0.34	0.18	0.35
pTau/βA	0.34	0.09	0.22	0.05	0.03	0.04
Serum Progranulin	172	n.p.	n.p.	116	71	130
Genetic	*C9ORF72*, *TARDP*, *MAPT* (negative) apoE (in progress)	E3/E3	n.p.	*C9ORF72*, *TARDBP* (negative) *MAPT* (in progress)	*C9ORF72* (positive) *E3/E3*	*C9ORF72*, *MAPT*, *TARDP* (negative)
Familial history	Negative	Negative	Negative	Mother with a similar clinical picture (onset 65 years)	Father with ALS	A maternal uncle with mood depression

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